CASE REPORT

Fish Malodour syndrome in a child

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SUMMARY

Body odour can be a manifestation of several metabolic diseases. Diagnosis may be difficult because the disease is often unknown to the doctor. We present a child observed in a general paediatric clinic for bad body odour after eating fish. Given the suspicion of trimethylaminuria, molecular study of flavin mono-oxygenase 3 gene was requested. A pathogenic mutation and polymorphism were identified, which could explain the complaint. Dietary and hygienic measures were imposed with symptom improvement.

BACKGROUND

Body odour is a frequent complaint, many times undervalued by doctors. But it can be the only manifestation of a metabolic disease. Trimethylaminuria, also known as Fish Malodour syndrome, is a rare condition, whose main feature is body odour resembling rotten fish.[1 2] The estimated prevalence is 1%, but it is underdiagnosed because doctors are unaware of this disease.[3] It is characterised by excessive excretion of trimethylamine (TMA) in the urine, sweat and other bodily secretions.[1–7] In normal situations, dietary precursors (trimethylamine-*N*-oxide (TMAO), lecithin, choline) are transformed to TMA by gut bacteria. TMA is transported to the liver, where it is oxidised by flavin mono-oxygenase 3 (FMO3) to odourless TMAO, which is excreted through bodily fluids (figure 1).[1]

Primary trimethylaminuria is caused by a functional defect of FMO3 that is inherited in an autosomal recessive manner.[7–9] Acquired/secondary trimethylaminuria has been described in patients with severe liver disease (major site of FMO3 activity) and chronic renal disease (consequence of bacterial overgrowth in the gut).[1 7]

Puberty, excessive sweating, menstruation, overload of sea fish or other food sources of TMA precursors, can increase the bad odour.[2 3] It can also be worsened by oral contraceptives and menopause.[4]

The main consequences are psychosocial with negative impact in personal, professional and social life.[2] Affected individuals may develop cleaning rituals, anxiety, social isolation, depression and even suicide.[5 9]

Physical examination is normal, except for the unpleasant body odour.[4] Diagnosis is based on clinical symptoms and biochemical urine analysis for TMA and TMAO with or without an oral challenge test, consisting of ingestion of large quantities of dietary precursors.[1–7] Molecular diagnosis with characterisation of mutations and polymorphisms related to this condition is also available.[1 2 5 7]

There is no definitive cure, although the adoption of some dietary and hygiene strategies can allow a relatively normal life.[4]

We present a case of a girl with bad body odour since the age of 12 months who, because of medical unawareness, was diagnosed with trimethylaminuria only at the age of 5.

The aim of this report is to alert doctors to this condition, in order to allow diagnose and a proper orientation that minimises psychological damage.

CASE PRESENTATION

A 5-year-old girl was observed in a general paediatric clinic of a Tertiary Paediatric Hospital with odour resembling rotten fish in her sweat and breath since the age of 12 months. The onset of symptoms coincided with the introduction of fish in her diet. The odour was stronger after eating hake, forkbeard or ling. Growth and development were normal. The child had a history of congenital hip dislocation with non-surgical correction at 4 months of age. Neither of the parents or other family members had similar symptoms. There was no parental consanguinity.

Clinical examination was normal, namely, no malodour or skin abnormalities were detected. But the child had not eaten fish the previous day.

The parents were very concerned about the situation and potential future social consequences. They had complained for many years to their general medical doctor who undervalued the situation. Owing to the parents' persisting worries, the child was sent for a paediatric consultation.

INVESTIGATIONS

Owing to the possibility of trimethylaminuria, a molecular study of the FMO3 gene was requested, since the biochemical urine analysis for TMA and TMAO was not available.

A pathogenic mutation in exon 4 in heterozigozity—p.P153L/N (c.458C>T/N) and a polymorphism p.E158K/N (c.472 G>A/N) also in heterozigozity were found. These findings implied that in situations of overload of dietary precursors of TMA (as found in fish), its oxidation would be compromised, causing excessive elimination in odorous form, responsible for the bad odour that the child presented after eating fish.

DIFFERENTIAL DIAGNOSIS

Since the child was healthy, with no symptoms besides the malodour after eating fish and clinical examination was also normal, other conditions such chronic liver disease, renal failure and genital infection were ruled out.

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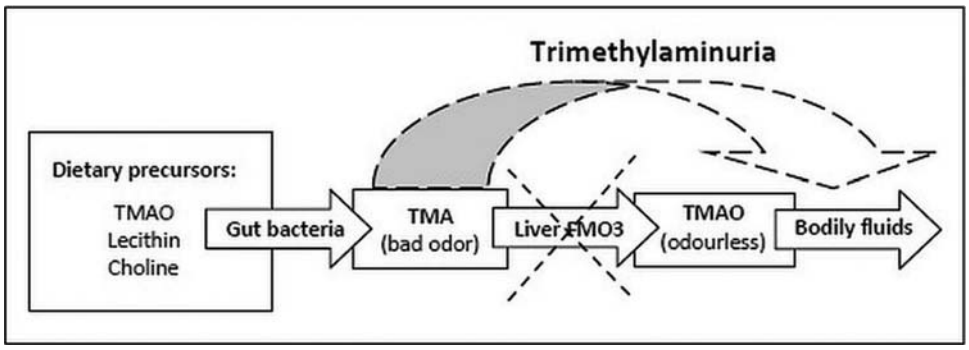

Figure 1 Normal metabolic pathway and pathway in trimethylaminuria (---). TMAO, trimethylamine-*N*-oxide; TMA, trimethylamine; FMO3, flavin mono-oxygenase 3.

TREATMENT

After confirmation of this clinical condition, the child and parents received guidance on hygiene and diet. Frequent washes with low pH soap and a diet with low contents of TMA precursors were suggested, especially before social and important events (but respecting daily needs inherent to sex and age). Ingestion of eggs, liver, cabbage, cauliflower, broccoli, Brussel's sprouts, turnips, sea fish, octopus, squid, cuttlefish, seafood, soy and soy products, peas, beans, peanuts and mustard would have to be limited.

OUTCOME AND FOLLOW-UP

With these measures there was a reduction of complaints.

DISCUSSION

Trimethylaminuria results from dysfunction of the FMO3 enzyme by genetic, hormonal factors and/or as a result of excessive substrate (excessive TMA diet precursors or changes in intestinal microflora).[1 2]

The FMO3 gene is very polymorphic. The P153L and E305X polymorphisms are responsible for severe cases.[2 3 5] Combinations of polymorphisms can be responsible for moderate and mild forms, causing decreased ability of enzymatic oxidation, especially when there is an overload of TMA diet precursors, as in this case.[1 2 6] The child only had symptoms when she ate fish, since it was present in her diet more frequently and in larger quantity than other food with precursors of TMA.

Trimethylaminuria is often associated with significant psychosocial disturbances, but other associations have been described: epilepsy (three case reports) and Prader-Willi syndrome (one case report).[10–12]

Therapy consists mainly of hygiene measures and food restriction. The use of low pH soap (to decrease the volatility of TMA) and the frequent washing of clothes are useful in eliminating bad odour.[1 4 5] Diet with restriction of TMA precursors, especially foods rich in choline (egg, liver, kidney, peas, peanuts, beans, broccoli), lecithin and TMAO (sea fish), has been more effective in mild to moderate conditions.[1–5 8 9 13 14] However, the recommended diet must satisfy the daily requirements of choline for age and sex. No restriction should be imposed during breastfeeding and pregnancy.[4 5] For short periods, antibiotic use (metronidazole or neomycin) has been helpful in some cases by decreasing intestinal microflora and the production of TMA.[1–4 6 9 13 14] Laxative use (such as lactulose) to accelerate gut transit with less TMA production by the intestinal microflora is also an alternative.[4 5] Dietary supplementation with riboflavin (FMO3 cofactor) may increase enzymatic activity.[4 5]

In circumstances where the production of TMA is increased (periods of stress, exercise, infection and menstruation) and a dietary restriction is not possible, these adjuvants have greater therapeutic value.[5 6]

Learning points

- Trimethylaminuria is an uncommon condition, but it has a high impact on the patient's life.
- Doctor awareness of this condition allows for a correct diagnosis.
- Implementation of food and hygiene strategies improves quality of life and minimises psychological consequences.

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Competing interests None.

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